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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,768	03/08/2005	R Rogers Yocum	OGZ-002US	9667

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EXAMINER	
FRONDA, CHRISTIAN L	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,768	YOCUM ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-49 and 83-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-49 and 83-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group IV (claims 34-49 and new claims 83-88) in the reply filed on 06/29/2007 is acknowledged. The traversal is on the ground(s) that the Kunst et al. reference fails to teach or suggest that the YaaD polypeptide is a B6 vitamer biosyntheitic polypeptide. Applicants' arguments have been considered but are not persuasive for reasons of record as supplemented below.

Sakai et al. (J Biosci Bioeng. 2002;93(3):309-12) provide evidence that YaaD and YaaE are involved in vitamin B6 biosynthesis in *Bacillus subtilis* (see entire publication). Furthermore, the instant specification shows that overexpression of the YaaD polypeptide results in over production of B6 vitamers (see Table 2, Table 5, Table 8).

Thus, the same or corresponding technical feature is not special since it was known in the prior art and therefore cannot make a contribution over the prior art. Since the inventions lack the same or corresponding special technical feature, then the inventions are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 34-49 and 83-88 are under consideration in this Office Action.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 33-49 and 83-88 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a microorganism transformed with a polynucleotide consisting of SEQ ID NO: 20 encoding a polypeptide consisting of SEQ ID NO: 21 and a polynucleotide consisting of SEQ ID NO: 22 encoding a polypeptide consisting of SEQ ID NO: 23 and production of B6 vitamers using said transformed microorganism; does not reasonably

provide enablement for any other embodiment as recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass methods for producing any B6 vitamer using any microorganism genetically modified to overexpress any gene that encodes any enzyme that catalyzes any step in the biosynthesis of any B6 vitamers, any gene encoding a polypeptide comprising an amino acid sequence which is at least 30% identical to SEQ ID NO: 21, and any gene encoding a polypeptide comprising an amino acid sequence which is at least 30% identical to SEQ ID NO: 23.

The specification provides guidance and working examples for *E. coli* host cells transformed with a polynucleotide consisting of SEQ ID NO: 20 encoding a polypeptide consisting of SEQ ID NO: 21 and a polynucleotide consisting of SEQ ID NO: 22 encoding a polypeptide consisting of SEQ ID NO: 23 and production of B6 vitamers using these transformed *E. coli* host cells.

However, the specification does not provide guidance, prediction, and working examples for any microorganism genetically modified to overexpress any gene that encodes any enzyme that catalyzes any step in the biosynthesis of any B6 vitamers, any gene encoding a polypeptide comprising an amino acid sequence which is at least 30% identical to SEQ ID NO: 21, and any gene encoding a polypeptide comprising an amino acid sequence which is at least 30% identical to SEQ ID NO: 23

Thus, an undue amount of trial and error experimentation must be preformed where such experimentation involves searching and screening a vast number of biological sources for any of the claimed polypeptides. Alternatively, trial and error experimentation must then be performed to search and screen for specific amino acid residues in SEQ ID NO: 21 and SEQ ID NO: 23 to change (e.g., amino acid deletion, insertion, substitution, and combinations thereof) which will not result in inactivation of the claimed polypeptide. General teaching regarding screening and searching for the claimed invention is not guidance for making the claimed invention.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and/or use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, such as information regarding the specific amino acid residues in SEQ ID NO: 21 and SEQ ID NO: 23 to

change which will not result in loss of enzyme activity, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

6. Claims 33-49 and 83-88 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to methods using a genus of microorganisms genetically modified to overexpress any gene that encodes any enzyme that catalyzes any step in the biosynthesis of any B6 vitamers. The scope of the genus includes many members with widely differing structural, chemical, and physiochemical properties including widely differing amino acid/nucleotide sequences and biological functions for the enzymes involved in B6 vitamer biosynthesis. Furthermore, the genus is highly variable because a significant number of structural and biological differences between genus members exist.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant application, the specification discloses *E. coli* host cells transformed with a polynucleotide consisting of SEQ ID NO: 20 encoding a polypeptide consisting of SEQ ID NO: 21 and a polynucleotide consisting of SEQ ID NO: 22 encoding a polypeptide consisting of SEQ ID NO: 23. The specification fails to disclose additional species as encompassed by the claimed genus, which are widely variant in their physiological characteristics, functions, and/or structures. As such the disclosure of the above mentioned *E. coli* host cells is insufficient to be representative of the attributes and features common to all the members of the claimed genus. Thus, one skilled in the art cannot visualize or recognize the identity of the members of the genus.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a

precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Therefore, the instant claims are not adequately described.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of a genus of microorganisms genetically modified to overexpress any gene that encodes any enzyme that catalyzes any step in the biosynthesis of any B6 vitamers.

The claims are additionally rejected for the following reasons. Gene elements which are not particularly described, including regulatory elements and untranslated regions, are essential to the function of the claimed invention since the claims recite genes involved in B6 vitamer biosynthesis including yaaD gene and yaaE gene. The art indicates that the structure of genes with regulatory elements and untranslated regions is empirically determined. Therefore, the structure of these elements which applicants considers as being essential to the function of the claim are not conventional in the art.

There is no known or disclosed correlation between the coding region of a polynucleotide encoding the YaaD or YaaE protein and the structure of the non-described regulatory elements and untranslated regions of the gene.

In view of the above considerations, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of any genes involved in B6 vitamer biosynthesis including yaaD gene and yaaE gene.

Claim Rejections - 35 U.S.C. § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 33-49 and 83-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moriya et al. (Accession D26185. 06-FEB-1999) in view of Sakai et al. (J Biosci Bioeng. 2001;91(2):147-52).

Moriya et al. (Accession D26185. 06-FEB-1999) teaches a polynucleotide comprising the nucleotide sequences of SEQ ID NO: 20 and SEQ ID NO: 22 encoding the yaaD polypeptide of SEQ ID NO: 21 and the yaaE polypeptide of SEQ ID NO: 23 (see SEQ ID NO: 20 Alignment, SEQ ID NO: 22 Alignment, SEQ ID NO: 21 Nucleotide Alignment, and SEQ ID NO: 23 Nucleotide Alignment).

Ogasawara et al. (Accession S66041; D69736. 28-OCT-1996) provide evidence that SEQ ID NO: 21 is the protein YaaD of *Bacillus subtilis* (see SEQ ID NO: 21 Protein Alignment). Ogasawara et al. (Accession S66042; E69736. 28-OCT-1996) provide evidence that SEQ ID NO: 23 is the protein YaaE of *Bacillus subtilis* (see SEQ ID NO: 23 Protein Alignment). Sakai et al. (J Biosci Bioeng. 2002;93(3):309-12) provide evidence that YaaD and YaaE are involved in vitamin B6 biosynthesis in *Bacillus subtilis* (see entire publication).

Moriya et al. do not teach a method for producing a B6 vitamer comprising culturing a genetically modified microorganism that overexpresses one or more genes encoding enzymes that catalyzes a step in the biosynthesis of a B6 vitamer.

Sakai et al. (J Biosci Bioeng. 2001;91(2):147-52) teach that *Bacillus subtilis* is a gram-positive bacterium that is important for industrial applications, and is one of the candidates for the host for microbial vitamin B6 production (see entire publication).

Thus, the recited method is obvious to one of ordinary skill in the art at the time the invention was made. It would have been obvious to transform *Bacillus subtilis* host cells to overexpress the polynucleotide encoding the B6 vitamer biosynthetic polypeptides YaaD and

YaaE taught by Moriya et al., respectively, and then culture the transformed host cell for production of B6 vitamers. One of ordinary skill in the art would be motivated to do this for the purposes of having a beneficial culturing method for ease of production of Vitamin B6, where Sakai et al. teach that *Bacillus subtilis* is important for industrial applications and is one of the candidates for the host for microbial vitamin B6 production. One of ordinary skill in the art would have a reasonable expectation of success for the production of each of the B6 vitamers recited in claims 39-41 since each of the YaaD and YaaE polypeptides are involved in vitamin B6 biosynthesis.

Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made, and was as a whole clearly prima facie obvious.

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

11. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000. CLF

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